Remarks

Claims 1-16 are pending in the present application and stand rejected. In this response, Applicants have canceled all claims and rewritten them as new claims 17-30.

With this response, Applicants are submitting under separate cover a certified translation of the German-language priority document DE 19903507.5, filed January 29, 1999. Applicants therefore request acknowledgment of priority under 35 U.S.C. §119 and assignment of a priority date of January 29, 1999.

The Office objects to claim 10 due to informalities concerning use of the term "obtainable." Applicants have canceled this claim; rendering this objection moot. Applicants therefore request that the objection be withdrawn.

Claims 1-9 and 11-16 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Claims 1-9 and 11-15 have been canceled and rewritten; claim 16 has been canceled. Applicants believe that these amendments, which are intended to improve readability and to conform the claims to standard U.S. practice, obviate the Office's rejection. Claim 1 no longer recites the phrase using the term "with" which was stated to be unclear in the Office Action. Further, the limitation "from the soluble fraction," now rewritten as "from said soluble fraction," has sufficient antecedent basis. Applicants have deleted the term "silica gel-like" from the claims and substituted the term "silicon dioxide." This amendment finds support throughout the application and specifically at, for example, page 3, lines 16-19 and page 9, lines 10-11. Claims 4, 7, 11, 12 and 13, which were specifically mentioned in the Action, are rewritten as new claims 20, 23, 26, 27 and 28. Applicants submit that these new claims

fully comply with 35 U.S.C. § 112, second paragraph and therefore request that the Office withdraw the rejection.

Claims 10-12 and 16 are rejected under 35 U.S.C. § 102(b) as anticipated by Horn et al. (*Human Gene Therapy* 6:565-573, 1995). As stated above, claim 16 has been canceled. Claim 10 also has been canceled. Claims 11-12 are rewritten as new claims 26-27. These claims now recite "a method of transfecting eukaryotic or prokaryotic cells" and "a method of producing a purified nucleic acid and/or oligonucleotide composition." Each claim contains positive method steps which are related to the steps of original claim 1, now rewritten as new claim 17.

The Horn et al. reference is cited by the Office for disclosing a method of producing highly purified eukaryotic plasmid expression vector useful for producing protein in *in vivo* gene therapy. The method for purifying low-endotoxin plasmid is described on page 567, cols. 1-2 as cited by the Examiner. This method is performed by lysing frozen bacteria, potassium acetate precipitation followed by filtration through Miracloth to remove cellular debris, precipitation of plasmid DNA with 2-propanol, collection and sedimentation of the precipitate, further precipitation with ammonium acetate, collection and filtration of the supernatant, and another precipitation with PEG-8000. The final precipitate is collected, resuspended, filtered and then subjected to gel filtration (size exclusion) and then ethanol precipitation for dilution and sterilization. See summary in Fig. 1, p. 569.

The Horn et al. reference therefore does not disclose, at any step, contacting the plasmid DNA with a silicon dioxide support material. The Sephacryl S-1000™ material in the Horn et al. columns is a dextran material, not a silicon dioxide or silica gel support. Further, Horn does not teach an alcohol

solution. To make out a case of anticipation, the Office must show that the cited reference contains, within its four corners, each and every limitation of the claims. M.P.E.P. § 2131. The claims here rejected require a silicon dioxide support incubation step and an alcoholic solution incubation step which are not taught or even suggested by Horn et al. Therefore, this reference cannot form the basis of either an anticipation or an obviousness rejection. Applicants therefore request the rejection be withdrawn.

Claims 10 and 16 are rejected under 35 U.S.C. § 102(b) as anticipated by Levison et al. or Prazeres et al. Both claims 10 and 16 have been canceled from this application. Applicants submit that this rejection is now moot and request its withdrawal.

Claims 10-12 and 16 are rejected under 35 U.S.C. § 102(e) as anticipated by Colpan et al. Claims 10 and 16 are canceled herein. Claims 11-12 are rewritten as new claims 26-27. Colpan et al. is cited as disclosing a process for isolating and purifying nucleic acids for use in gene therapy that involves potassium acetate and removal of endotoxins. Applicants respectfully submit that this reference does not anticipate the claims of this application. Colpan et al. do not teach a method as claimed here. The Colpan et al. method uses, as a first step, filtration by passing lysate through a filter material that may include silica gel in some embodiments. Elution is followed by an alcohol precipitation to produce the final product, a pellet which is dissolved in Tris-EDTA buffer. This reference does not involve a potassium acetate precipitation step, which is required by the claims rejected here. Nor does it discuss, prior to contacting with its "filtration material" using an alcohol solution to precipitate and then using the supernatant to proceed

with purification of nucleic acids. Colpan et al. use a low concentration alcohol-containing buffer during "filtration" and after filtration an alcohol precipitation where the desired nucleic acids form the pellet. See, e.g., Example 1. These two methods are not the same and do not use the same methods. Since Colpan et al. do not teach or suggest each and every limitation of the rewritten claims, Applicants respectfully suggest that the Office cannot meet its burden to establish anticipation by the Colpan et al. reference. Applicants therefore request that the Office withdraw the rejection of claims 26-27 on this basis.

Claims 10-11 and 16 are rejected under 35 U.S.C. § 102(e) as anticipated by Smith et al. Claims 10 and 16 are canceled herein. Claim 11 is rewritten as new claim 26. The Smith et al. method is described in the Office Action as including mixing a prepurified biological sample with potassium acetate and as resulting in nucleic acids free of endotoxin and suitable for administration to organisms. The Smith et al. methods involve preparation of a cleared lysate using potassium acetate precipitation (Example 1), followed by a two-step silica procedure, a preferred embodiment of which is outlined in Example 10. In the first silica step, the cleared lysate supernatant is incubated with silica particles (in diluted potassium acetate buffer) and then the silica separated from the solution. The lysate then is incubated with silica in the presence of high concentration of a chaotropic salt, after which the lysate is discarded. The silica then is washed with an ethanol solution and then heated. The bound plasmid DNA is eluted with water.

Smith et al. do not teach treatment of a potassium acetate precipitation supernatant with an alcoholic solution with reservation of the resulting supernatant for later fractionation using silicon dioxide. Alcohol is only used as a wash of the

silica in Smith et al., demonstrating that the desired nucleic acids are not eluted by and therefore do not become dissolved in the alcohol solution as they are in claim 26, step (a)(6). A careful comparison of the claim to the disclosures of Smith et al. shows that Smith et al. do not teach, or even suggest, each and every limitation of claim 26, particularly steps (a)(4) through (a)(6). Applicants therefore submit that the rejection of claim 26 over this reference is not proper and request its withdrawal.

For the reasons discussed above and in light of the amendments made herein, Applicants now request favorable consideration of the present application.

RESPECTFULLY SUBMITTED,					
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